

REMARKS/ARGUMENTS

Applicants respectfully request reconsideration and allowance of this application in view of the amendments above and the following comments.

Claim 12 has been amended without prejudice to specify that the “ligands” are “antibodies” and, also, that the antibodies specifically bind to either (i) the CD4 and CTLA-4 entities on the T cells or (ii) the CD25 and CTLA-4 entities on the T cells. These amendments find clear support in the specification, for example, at page 4, lines 25-29. In this regard, Applicants respectfully submit that recitation in the specification of the limited class “CD4, and/or CD25, and/or CTLA-4” provides written description support for all seven member embodiments falling thereunder, those being (i) CD4, (ii) CD25, (iii) CTLA-4, (iv) CD4 + CD25, (v) *CD4 + CTLA-4*, (vi) *CD25 + CTLA-4* and (vii) CD4 + CD25 + CTLA-4.

Editorial amendments have been made to claim 28 to make it consistent with amended claim 12.

Finally, claim 33 has been amended to revise step (c) to require that the isolated CD4+CD25+ T cells isolated in step (b) are tested for constitutive expression of CTLA-4. Such language is supported, for example, by page 21, lines 11-13 and 27-29.

Applicants do not believe that any of the amendments introduce new matter. An early notice to that effect is earnestly solicited.

Claims 12 and 25-32 were rejected under 35 USC § 112, first paragraph, as failing to comply with the written description requirement. In response, Applicants point out that, as noted

above, claim 12 has been amended without prejudice to specify the “ligands” are “antibodies.” The Examiner concedes written description support for antibodies at the bottom of page 3 of the Office Action (i.e., “the specification * * * discloses * * * CD4, CD25, or CTLA-4 specific antibodies.”) Accordingly, Applicants respectfully submit that this rejection is overcome by the amendments to claim 12.

Claims 12, 24-29 and 33 were rejected under 35 USC § 102(b) as being anticipated by Koulis et al. (“Koulis”), *J. Allergy Clin. Immunol.*, 107: S294-S295 (2001), as evidenced by Miltenyi Biotec product information (2007). In response, Applicants would remind the Examiner that anticipation requires that each and every element as set forth in the claim must be found, either expressly or inherently described, in a single prior art reference, and, further, the absence in the prior art reference of even a single one of the claim elements is sufficient to negate anticipation. *In re Robertson*, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999). Koulis is silent about the significance of CTLA-4 expression and, therefore, does not teach either step (a) of claim 12 or step (c) of claim 33. Consequently, Koulis cannot anticipate the present claims.

In view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw this rejection. An early notice that this rejection has been reconsidered and withdrawn is earnestly solicited.

Claims 12, 24-30, 32 and 33 were rejected under 35 USC § 103(a) as being obvious over Koulis in view of Thornton et al. (“Thornton”), *J. Exp. Med.*, 188: 287-296 (1998). In response, Applicants point out that this rejection was premised on Koulis anticipating the broad aspects of main claim 12, which Applicants have shown above is not, in fact, the case. Nothing in

Thornton overcomes the above-noted deficiencies in Koulis. Indeed, Thornton is relied upon to teach the contact-dependent nature of regulatory T cell suppression and the expected cytokine profile. However, nothing in the combination of Koulis and Thornton teaches or suggests the importance of CTLA-4 expression. Consequently, the combination of Koulis and Thornton fails to make out a *prima facie* case of the obviousness of the rejected claims.

In view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw this rejection as well. An early notice that this rejection has been reconsidered and withdrawn is also earnestly solicited.

Claim 31 was rejected under 35 USC § 103(a) as being obvious over Koulis in view of Thornton and further in view of Stout et al. ("Stout"), *J. Immunol.*, 150: 5330-5337 (1993). In response, Applicants point out that this rejection also was premised on Koulis anticipating the broad aspects of main claim 12, which Applicants have shown above is not, in fact, the case. Nothing in the combination of Thornton and Stout overcomes the above-noted deficiencies in Koulis. Indeed, as noted above, Thornton is relied upon to teach the contact-dependent nature of regulatory T cell suppression and the expected cytokine profile. Stout is relied on to teach the regulatory properties of fixed cells. However, nothing in the combination of Koulis and Thornton with Stout teaches or suggests the importance of CTLA-4 expression. Consequently, the combination of Koulis and Thornton with Stout also fails to make out a *prima facie* case of the obviousness of the rejected claim.

In view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw this rejection as well. An early notice that this rejection has been reconsidered and withdrawn is also earnestly solicited.

Applicants believe that the foregoing constitutes a bona fide response to all outstanding objections and rejections.

Applicants also believe that this application is in condition for immediate allowance. However, should any issue(s) of a minor nature remain, the Examiner is respectfully requested to telephone the undersigned at telephone number (212) 808-0700 so that the issue(s) might be promptly resolved.

Early and favorable action is earnestly solicited.

Respectfully submitted,
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